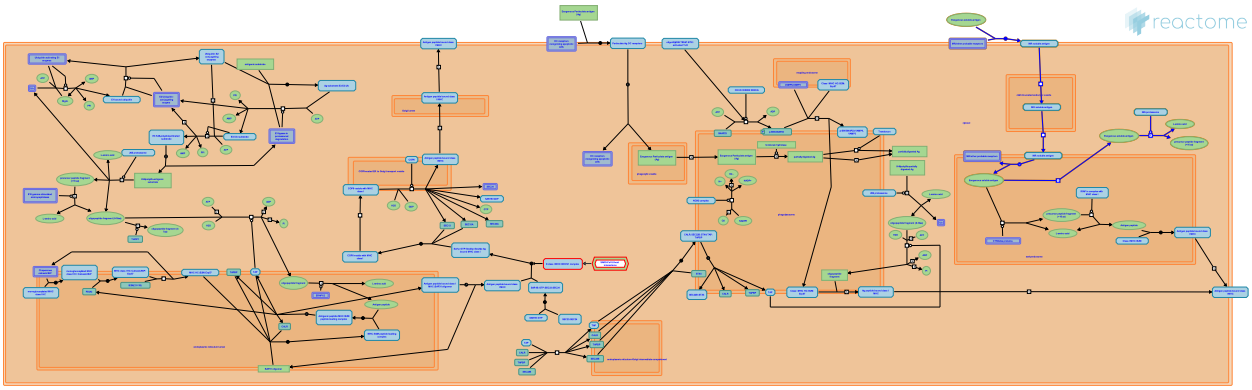
Cross-presentation of soluble exogenous antigens (endosomes)



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06/05/2024

Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.
The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

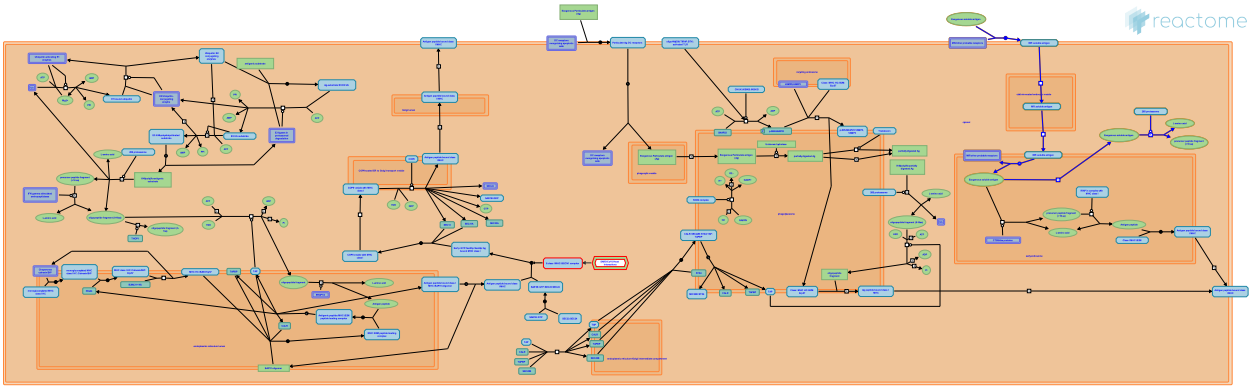
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Cross-presentation of soluble exogenous antigens (endosomes)

Stable identifier: R-HSA-1236978



Exogenous soluble antigens are cross-presented by dendritic cells, albeit with lower efficiency than for particulate substrates. Soluble antigens destined for cross-presentation are taken up by distinct endocytosis mechanisms which route them into stable early endosomes and then to the cytoplasm for proteasomal degradation and peptide loading.

Literature references

Savina, A., Amigorena, S. (2010). Intracellular mechanisms of antigen cross presentation in dendritic cells. *Curr Opin Immunol, 22*, 109-17.

Trombetta, ES., Monu, N. (2007). Cross-talk between the endocytic pathway and the endoplasmic reticulum in cross-presentation by MHC class I molecules. *Curr Opin Immunol, 19*, 66-72.

Ackerman, AL., Kyritsis, C., Cresswell, P., Tampé, R. (2005). Access of soluble antigens to the endoplasmic reticulum can explain cross-presentation by dendritic cells. *Nat Immunol, 6*, 107-13.

Editions

2011-03-28	Authored, Edited	Garapati, P V.
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Interaction of exogenous soluble antigen with its corresponding receptor ↗

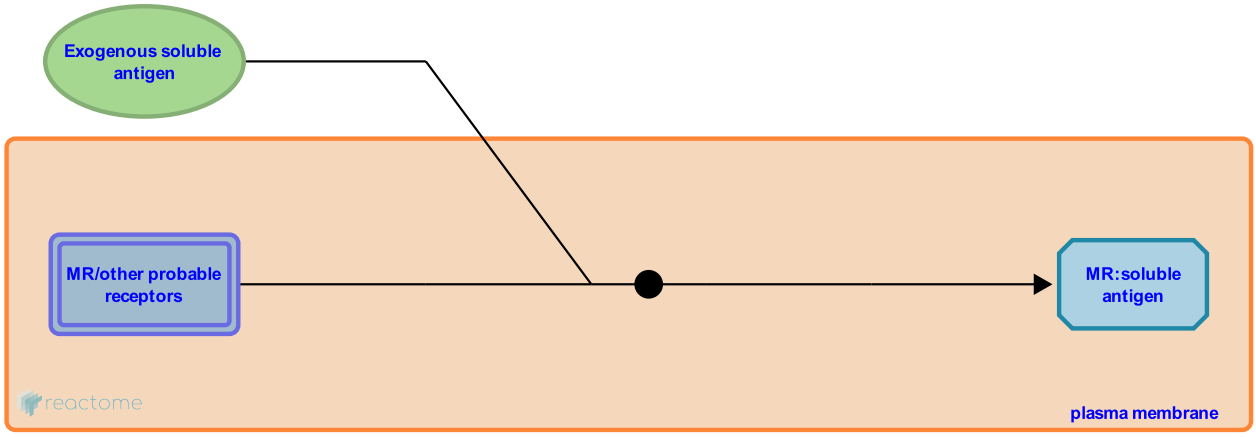
Location: Cross-presentation of soluble exogenous antigens (endosomes)

Stable identifier: R-HSA-1236939

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: Interaction of soluble ovalbumin with mannose receptor (Gallus gallus)



Soluble antigens are presented to dendritic cells (DCs) in some cases by receptor mediated endocytosis or fluid-phase endocytosis. Burgdorf et al. (2008) suggest that there are two different endocytic compartments for antigen processing: one dedicated to MHC class I (early endosomes) and the other one for MHC class II presentation (lysosomes). Sorting of cargo into these different compartments occurs at the plasma membrane and is likely to depend on the type of endocytic receptor the cargo is interacting with (Burgdorf et al. 2008, Zhuang et al. 2006). The mannose receptor (MR) is the best studied receptor that targets soluble antigens to early endosomes but not to lysosomes (Burgdorf et al. 2006). Antigens taken up by the MR are targeted towards a mildly acidic stable early endosomal compartment for exclusive presentation on MHC I molecules (Burgdorf et al. 2008).

Followed by: Internalization of receptor bound antigen into clathrin coted vesicles

Editions

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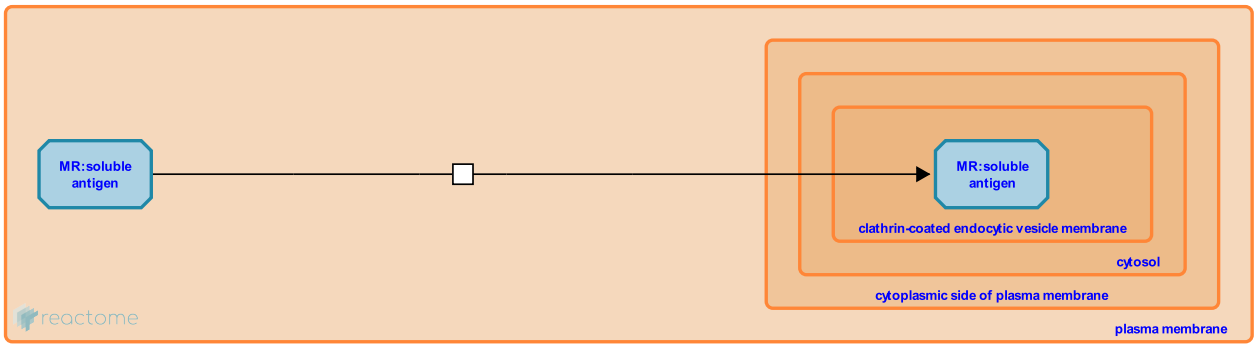
Internalization of receptor bound antigen into clathrin coted vesicles ↗

Location: Cross-presentation of soluble exogenous antigens (endosomes)

Stable identifier: R-HSA-1236941

Type: transition

Compartments: plasma membrane, extracellular region, clathrin-coated endocytic vesicle membrane



Receptor-bound exogenous antigens in coated pits on the cell surface are internalized into clathrin-coated vesicles.

Preceded by: Interaction of exogenous soluble antigen with its corresponding receptor

Followed by: Movement of clathrin coated vesicles into early endosome

Literature references

Kurts, C., Burgdorf, S. (2008). Endocytosis mechanisms and the cell biology of antigen presentation. *Curr Opin Immunol, 20*, 89-95. ↗

Botelho, RJ., Vieira, OV., Grinstein, S. (2002). Phagosome maturation: aging gracefully. *Biochem J, 366*, 689-704. ↗

McMahon, HT., Doherty, GJ. (2009). Mechanisms of endocytosis. *Annu Rev Biochem, 78*, 857-902. ↗

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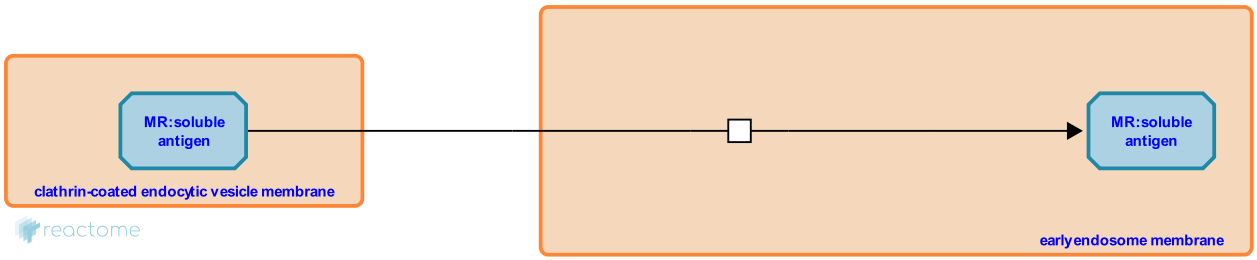
Movement of clathrin coated vesicles into early endosome ↗

Location: Cross-presentation of soluble exogenous antigens (endosomes)

Stable identifier: R-HSA-1236955

Type: transition

Compartments: early endosome membrane, clathrin-coated endocytic vesicle membrane



The antigen:receptor complex moves from clathrin-coated vesicles to the early endosome membrane.

Preceded by: Internalization of receptor bound antigen into clathrin coted vesicles

Followed by: Exogenous soluble antigen targeted to more stable early endosome

Literature references

Botelho, RJ., Vieira, OV., Grinstein, S. (2002). Phagosome maturation: aging gracefully. *Biochem J, 366*, 689-704. ↗

McMahon, HT., Doherty, GJ. (2009). Mechanisms of endocytosis. *Annu Rev Biochem, 78*, 857-902. ↗

Editions

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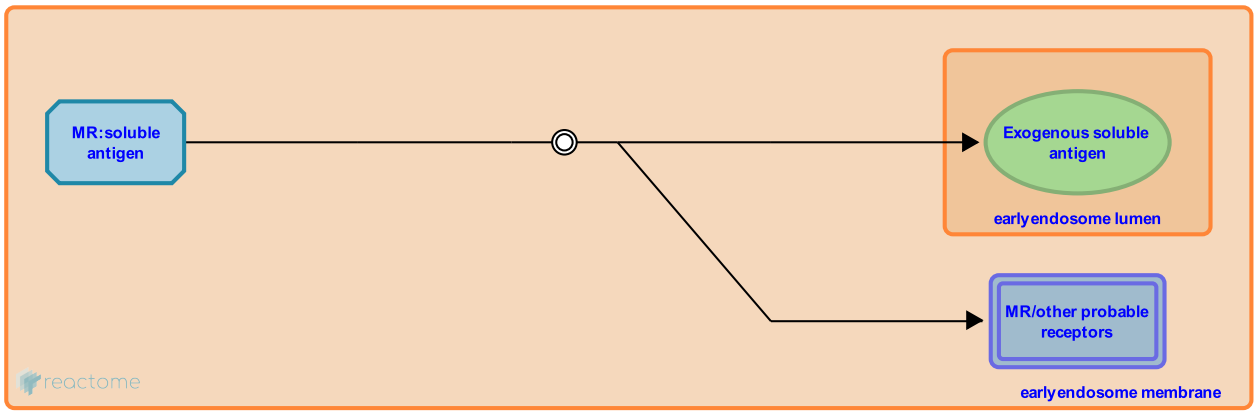
Exogenous soluble antigen targeted to more stable early endosome ↗

Location: Cross-presentation of soluble exogenous antigens (endosomes)

Stable identifier: R-HSA-1236940

Type: dissociation

Compartments: early endosome membrane, early endosome lumen



Within the endosome the receptor and cargo separate and the receptor recycles back to the cell surface. Soluble antigens are targeted into the stable early endosome lumen for efficient cross presentation. Early endosomes are mildly acidic and relatively poor in proteases.

Preceded by: Movement of clathrin coated vesicles into early endosome

Followed by: Egress of internalized antigen into cytosol from early endosome

Literature references

Ackerman, AL., Kyritsis, C., Cresswell, P., Tampé, R. (2005). Access of soluble antigens to the endoplasmic reticulum can explain cross-presentation by dendritic cells. *Nat Immunol, 6*, 107-13. ↗

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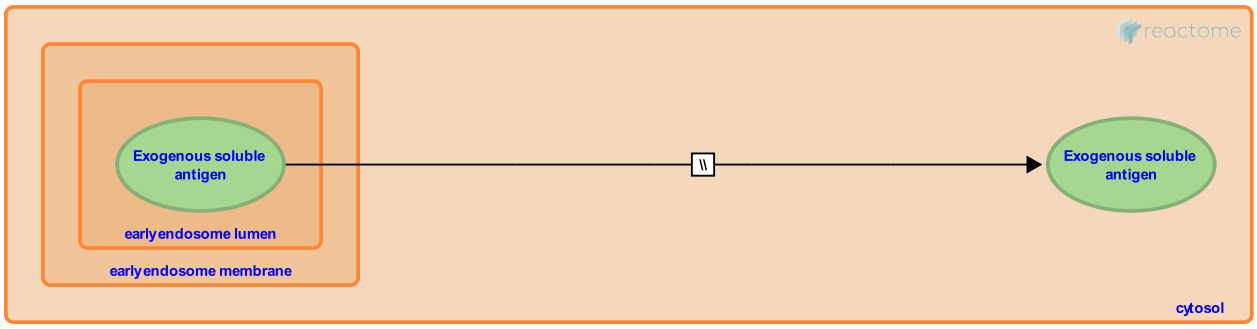
Egress of internalized antigen into cytosol from early endosome ↗

Location: Cross-presentation of soluble exogenous antigens (endosomes)

Stable identifier: R-HSA-1236968

Type: omitted

Compartments: cytosol, early endosome lumen



Endocytosed antigens must leave the endocytic structure to enter into the MHC I pathway before exhaustive degradation within lysosomes. The canonical pathway is the transporter associated with antigen processing (TAP)-dependent cytosolic pathway, which involves the translocation of endocytosed antigens into the cytosol where they are degraded into antigenic peptides by the proteasome and transported to ER through TAP. This hypothesis comes from indirect evidences showing that proteasome inhibitors block cross presentation of certain antigens (Amigorena et al. 2010, Burgdorf et al. 2008) . According to this model antigens are translocated into the cytosol by an undefined mechanism.
There are less well-characterized mechanisms for the delivery of exogenous antigens into the cytosol. Certain peptides with highly positively charged sequences derived from HIV tat protein or the Antennapedia homeodomain (AntHD) protein seem to penetrate into the cytosol directly across the plasma membrane (Monu et al. 2007, Vendeville et al. 2004). It is also proposed that some exogenous antigens can be exchanged between neighboring cells through gap junctions, leading to cross presentation by the recipient cell (Monu et al. 2007, Neijssen et al. 2005).
Once internalized antigens are routed into the cytosol, they follow the conventional pathway of proteasome digestion and TAP mediated transport of peptides into the ER lumen.

Preceded by: Exogenous soluble antigen targeted to more stable early endosome

Followed by: Proteasomal clevage of exogenous antigen

Literature references

Zhuang, X., Rust, MJ., Lakadamyali, M. (2006). Ligands for clathrin-mediated endocytosis are differentially sorted into distinct populations of early endosomes. *Cell, 124*, 997-1009. ↗

Rodriguez, A., Regnault, A., Ricciardi-Castagnoli, P., Amigorena, S., Kleijmeer, M. (1999). Selective transport of internalized antigens to the cytosol for MHC class I presentation in dendritic cells. *Nat Cell Biol, 1*, 362-8. ↗

Nolan, GP., Kim, DT., Fathman, CG., Brockstedt, DG., Mitchell, DJ., Rothbard, JB. et al. (1997). Introduction of soluble proteins into the MHC class I pathway by conjugation to an HIV tat peptide. *J Immunol, 159*, 1666-8. ↗

Trombetta, ES., Pack, M., Mellman, I., Chang, H., Delamarre, L. (2005). Differential lysosomal proteolysis in antigen-presenting cells determines antigen fate. *Science, 307*, 1630-4. ↗

Rayne, F., Vendeville, A., Montcourrier, P., Beaumelle, B., Bonhoure, A., Bettache, N. (2004). HIV-1 Tat enters T cells using coated pits before translocating from acidified endosomes and eliciting biological responses. *Mol Biol Cell, 15*, 2347-60. ↗

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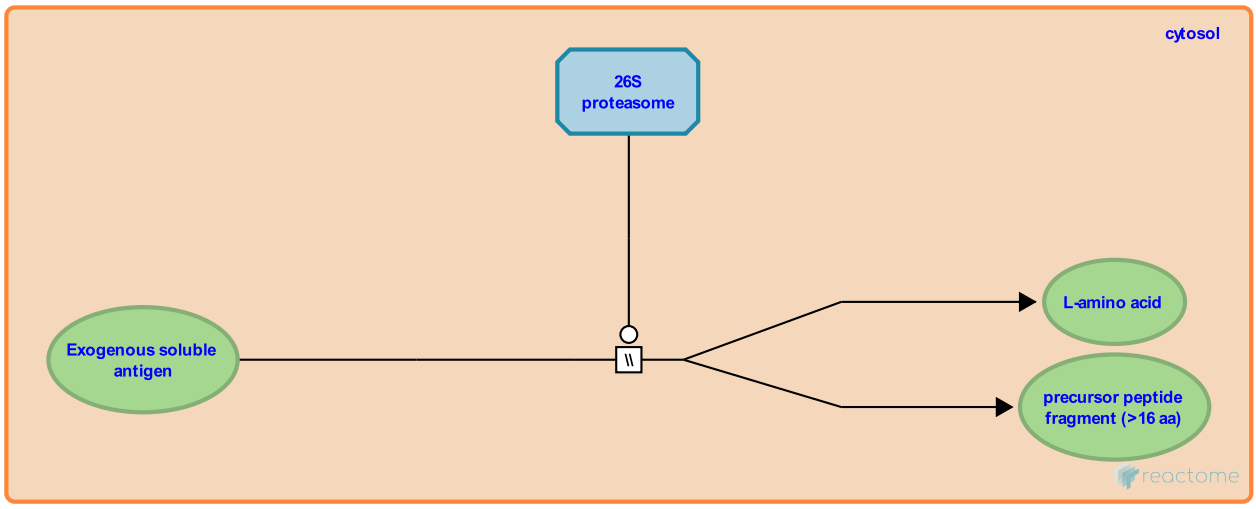
Proteasomal clevage of exogenous antigen ↗

Location: Cross-presentation of soluble exogenous antigens (endosomes)

Stable identifier: R-HSA-1236970

Type: omitted

Compartments: cytosol



Exogenous antigens are thought to be processed for cross-presentation in much the same manner as endogenous proteins once they enter the cytosolic pathway (Rock et al. 2010). Immunoproteasome components are the major proteases involved in generating the antigenic fragments. The precurssor peptides are further trimmed by cytosolic aminopeptidases and shuttled to ER through TAP for MHC class I loading.

Preceded by: Egress of internalized antigen into cytosol from early endosome

Literature references

Addey, C., Millrain, M., Gallimore, A., Scott, D., Cerundolo, V., Dyson, J. et al. (2006). Role of immunoproteasomes in cross-presentation. *J Immunol, 177*, 983-90. ↗

Rock, KL., Farfán-Arribas, DJ., Shen, L. (2010). Proteases in MHC class I presentation and cross-presentation. *J Immunol, 184*, 9-15. ↗

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